On page 6, line 34, please delete "Figure 40 shows" and replace with: --Figures 40(A) and 40(B) show--

On page 7, line 1, please delete "Figure 41 shows" and replace with: --Figures 41(A) and 41(B) show--

On page 7, line 5, please delete "Figure 42(A) shows" and replace with: --Figures 42(A) and 42(B) show--

On page 7, line 10, please delete "Figure 42 (B) shows" and replace with: --Figures 42(C) and 42(D) show--

On page 7, line 14, please delete "Figure 42 (C) shows" and replace with: --Figure 42(E) shows--

REMARKS

Applicants respectfully request entrance of the amendments as detailed above, in the continuation application filed herewith under 37 C.F.R. § 1.53(b). Applicants respectfully submit that the continuation application filed herewith on June 5, 2001, is co-pending with application number 08/986,025, now Patent No.: 6,242,469, which issued on the same date (June 5, 2001) that this continuing application is being filed. See MPEP § 201.11 which states "If the first application issues as a patent, it is sufficient for the second application to be co-pending with it if the second application is filed *on the same date*, or before the date that the patent issues on the first application."

Applicants respectfully submit that no new matter is presented with these amendments. Rather, the original specification, as filed on December 3, 1997, has been provided for filing under 37 C.F.R. §1.53 (b), and Applicants respectfully submit that this preliminary amendment is requested to correct formal matters in the specification (e.g., addition of a statement of continuation application status (with incorporation by reference), addition of a statement regarding government support, and ensuring consistency between the specification and formal drawings). As required, Applicants have submitted herewith replacement sections and paragraphs for those sections and paragraphs that have been amended as detailed above.

listed as Dang Fang Meng. Applicants respectfully submit that the correct spelling is **Dongfang Meng**. As set forth in MPEP 605.04(b), "when a typographical or transliteration error in the spelling of an inventor's name is discovered during the pendency of an application, a petition is not required, nor is a new oath or declaration under 37 CFR 1.63 needed". Applicants thus respectfully request that reference is made to this notification on the declaration so that any further correspondence (e.g., filing receipts) and issued patents will reflect the correct spelling of his name.

Applicants would like to thank the Examiner in advance for review of this request. If it is believed that a telephone conversation would expedite matters, the Examiner is invited to contact the undersigned at (617) 248-5216. The Examiner's attention is also directed to the recent change in power of attorney and correspondence address, as submitted herewith. Although it is believed that there is no fee associated with this amendment, if Applicants are mistaken, please charge any fees to our Deposit Account No.: 03-1721.

Respectfully Submitted,

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Danishefsky *et al.*	Examiner: T. Solola
Serial No.:	not yet assigned	Group Art Unit: 1626
Filed:	June 5, 2001	
For:	*Synthesis of Epothilones, Intermediates Thereto, Analogues and Uses Thereof*	

EXPRESS MAIL NO.: EL603009699US

Paragraph and Section Replacements for Preliminary Amendment

A) A replacement paragraph is provided below, which paragraph begins on page 1, line 27 and ends on page 1, line 34.

This application is a continuation application filed under 37 C.F.R. § 1.53(b) of application number 08/986,025, filed December 3, 1997, and issued as U.S. Patent No.: 6,242,469 on June 5, 2001, the entire contents of which are hereby incorporated by reference, which is based on U.S. Provisional Application Serial Nos. 60/032,282, 60/033,767, 60/047,566, 60/047,941, and 60/055,533, filed December 3, 1996, January 14, 1997, May 22, 1997, May 29, 1997, and August 13, 1997, respectively, the contents of which are hereby incorporated by reference into this application. This invention was made with government support under grants CA-28824, CA-39821, CA-GM 72231, CA-62948, and AI0-9355 from the National Institutes of Health, and grant CHE-9504805 from the National Science Foundation. Additionally, the present invention was supported in part by a fellowship from the United States Army to Dongfang Meng (DAMD 17-97-1-7146), and thus the government has certain rights in the invention.

B) A replacement section is provided below, which section begins on page 3, line 21 and ends on page 3, line 22

Figures 3(A) and 3(B) provide syntheses of key iodinated intermediates used to prepare hydroxymethylene- and hydroxypropylene-substituted epothilone derivatives.

C) A replacement section is provided below, which section begins on page 3, line 24 and ends on page 3, line 27.

Figures 3(C) and 3(D) provide methods of preparing hydroxymethylene- and hydroxypropylene-substituted epothilone derivatives, said methods being useful generally to prepare 12,13-E epothilones wherein R is methyl, ethyl, n-propyl, and n-hexyl from the corresponding E-vinyl iodides.

D) A replacement section is provided below, which section begins on page 3, line 29 and ends on page 3, line 30.

Figures 3(E) and 3(F) show reactions leading to benzoylated hydroxymethyl-substituted desoxyepothilone and hydroxymethylene-substituted epothilone (epoxide).

E) A replacement section is provided below, which section begins on page 4, line 9 and ends on page 4, line 9.

Figures 6(A) and 6(B) provide a scheme of an olefin metathesis route to epothilone A and other analogues.

F) A replacement section is provided below, which section begins on page 4, line 29 and ends on page 4, line 29.

Figures 14(A) and 14(B) show the preparation of intermediate **4A**.

Figures 18(A) and 18(B) provide a synthetic pathway to a protected intermediate for 8-desmethyl deoxyepothilone A.

H) A replacement section is provided below, which section begins on page 5, line 10 and ends on page 5, line 11.

Figures 19(A), 19(B), and 19(C) provide a synthetic pathway to 8-desmethyl deoxyepothilone A and a trans-iodoolefin intermediate thereto.

I) A replacement section is provided below, which section begins on page 5, line 13 and ends on page 5, line 22.

Figure 20(A) shows structures of epothilones A and B and 8-desmethylepothilone and Figure 20(B) shows a synthetic pathway to intermediate TBS ester **10** used in the preparation of desmethylepothilone A. (a) (Z)-Crotyl-B[(-)-Ipc]$_2$, -78°C, Et_2O, then 3 N NaOH, 30% H_2O_2; (b) TBSOTf, 2,6-lutidine, CH_2Cl_2 (74% for two steps, 87% ee); (c) O_3, CH_2Cl_2/MeOH, -78°C, then DMS, (82%); (d) t-butyl isobutyrylacetate, NaH, BuLi, 0°C, then **6** (60%, 10:1); (e) $Me_4NBH(OAc)_3$, -10°C (50%, 10:1 α/β) or $NaBH_4$, MeOH, THF, 0°C, (88%, 1:1 α/β); (f) TBSOTf, 2,6-lutidine, -40°C, (88%); (g) Dess-Martin periodinane, (90%); (h) $Pd(OH)_2$, H_2, EtOH (96%); (l) DMSO, oxalyl chloride; CH_2Cl_2, -78°C (78%); (j) Methyl triphenylphosphonium bromide, NaHMDS, THF, 0°C (85%); (k) TBSOTf, 2,6-lutidine, CH_2Cl_2, rt (87%).

J) A replacement section is provided below, which section begins on page 5, line 29 and ends on page 5, line 29.

Figures 22(A), 22(B) and 22(C) show a synthetic pathway to prepare epothilone analogue

K) A replacement section is provided below, which section begins on page 5, line 31 and ends on page 5, line 31.

Figures 23(A), 23(B) and 23(C) show a synthetic pathway to prepare epothilone analogue **24D**.

L) A replacement section is provided below, which section begins on page 5, line 33 and ends on page 5, line 33.

Figures 24(A) and 24(B) show a synthetic pathway to prepare epothilone analogue **19D**.

M) A replacement section is provided below, which section begins on page 5, line 35 and ends on page 5, line 35.

Figures 25(A), 25(B), 25(C) and 25(D) show a synthetic pathway to prepare epothilone analogue **20D**.

N) A replacement section is provided below, which section begins on page 5, line 37 and ends on page 5, line 37.

Figures 26(A), 26(B), 26(C) and 26(D) show a synthetic pathway to prepare epothilone analogue **22D**.

O) A replacement section is provided below, which section begins on page 6, line 1 and ends on page 6, line 2.

Figures 27(A), 27(B) and 27(C) show a synthetic pathway to prepare epothilone analogue 12-hydroxy ethyl epothilone.

page 6, line 7.

Figures 28(A) and 28(B) show the activity of epothilone analogues in a sedimentation test in comparison with DMSO, epothilone A and/or B. Structures 17-20, 22, and 24-27 are shown in Figures 29-37, respectively. Compounds were added to tubulin (1 mg/ml) to a concentration of 10 μM. The quantity of microtubules formed with epothilone A was defined as 100%.

Q) A replacement section is provided below, which section begins on page 6, line 30 and ends on page 6, line 32.

Figures 39(A) and 39(B) show epothilone A and epothilone analogues #1-7. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

R) A replacement section is provided below, which section begins on page 6, line 34 and ends on page 6, line 36.

Figures 40(A) and 40(B) show epothilone B and epothilone analogues #8-16. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

S) A replacement section is provided below, which section begins on page 7, line 1 and ends on page 7, line 3.

Figures 41(A) and 41(B) show epothilone analogues #17-25. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

page 7, line 7.

Figures 42(A) and 42(B) show epothilone analogues #26-34. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

U) A replacement section is provided below, which section begins on page 7, line 10 and ends on page 7, line 12.

Figures 42(C) and 42(D) show epothilone analogues #35-46. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

V) A replacement section is provided below, which section begins on page 7, line 14 and ends on page 7, line 14.

Figures 42(E) shows epothilone analogues #47-49.

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